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Hepatitis C virus among blood donors and general population in Middle East and North Africa: Meta-analyses and meta-regressions

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Abstract

BACKGROUND

Despite the Middle East and North Africa (MENA) Region reported to have the highest prevalence of hepatitis C virus (HCV) globally, HCV infection levels in the majority of MENA countries remain inadequately characterized. Blood donor data have been previously used as a proxy to assess levels and trends of HCV in the general population, however, it is unclear how comparable these populations are in MENA and whether blood donors provide an appropriate proxy.

AIM

To delineate HCV epidemiology among blood donors and the general population in the MENA.

METHODS

The data source was the systematically gathered MENA HCV Epidemiology Synthesis Project Database. Random-effects meta-analyses and meta-regressions were conducted. For comparison, analyses were conducted for Europe, utilizing the Hepatitis C Prevalence Database of the European Centre for Disease Prevention and Control.

RESULTS

One thousand two hundred and thirteen HCV antibody prevalence measures and 84 viremic rate measures were analyzed for MENA. Three hundred and seventy-seven antibody prevalence measures were analyzed for Europe. In MENA, pooled mean prevalence was 1.58% [95% confidence interval (CI): 1.48%–1.69%] among blood donors and 4.49% (95%CI: 4.10%–4.90%) in the general population. In Europe, pooled prevalence was 0.11% (95%CI: 0.10%–0.13%) among blood donors and 1.59% (95%CI: 1.25%–1.97%) in the general population. Prevalence in the

general population was 1.72-fold (95%CI: 1.50–1.97) higher than that in blood donors in MENA, but it was 15.10-fold (95%CI: 11.48–19.86) higher in Europe. Prevalence was declining at a rate of 4% per year in both MENA and Europe [adjusted risk ratio: 0.96 (95%CI: 0.95–0.97) in MENA and 0.96 (95%CI: 0.92–0.99) in Europe]. Pooled mean viremic rate in MENA was 76.29% (95%CI: 67.64%–84.02%) among blood donors and 65.73% (95%CI: 61.03%–70.29%) in the general population.

CONCLUSION
Blood donor data provide a useful proxy for HCV infection in the wider population in MENA, but not Europe, and could improve HCV burden estimations and assess progress toward HCV elimination by 2030.

Key Words: Hepatitis C virus; Viral hepatitis; Blood donors; General population; Middle East and North Africa; Meta-analysis; Meta-regression

Core tip: We investigated hepatitis C virus (HCV) epidemiology among blood donors and the wider general population in Middle East and North Africa (MENA). For comparison, similar analyses were performed for Europe. Our results indicated that HCV antibody prevalence in the population of MENA and Europe appears to be declining by 4% per year. Blood donor data in MENA (but not in Europe) were found to provide a useful proxy for HCV infection levels and trends in the general population. Thus, the data can be utilized in HCV estimates and to assess, track and validate progress towards World Health Organization elimination goals for HCV.

INTRODUCTION

In the Middle East and North Africa (MENA) an estimated 15 million individuals are chronically infected with hepatitis C virus (HCV), making it the global region most affected by HCV infection[1]. Left untreated, chronic HCV infection may lead to several morbidities, including liver cancer, fibrosis, and cirrhosis[2]. Prompted by development of highly efficacious direct-acting antivirals (DAAs), the World Health Organization (WHO) has set a global target to eliminate HCV as a public health problem by 2030[3].

Despite disproportionally high HCV infection levels in specific MENA countries, *e.g.*, Egypt[4-7] and Pakistan[8-11], relative to global levels[1,12], only three countries in this region have conducted nationally representative population-based surveys[13-15]. HCV infection levels in the remaining countries remain inadequately characterized[1].

Blood donors have been used as a proxy population to provide a crude estimate of HCV infection levels in the general population[16,17]. However, in developed countries, such as the United States[18] and countries of the European Union[16], blood donors are not considered representative of the wider general population. In these countries, strict donor selection and blood safety regulations[19] have resulted in a large disparity in HCV infection levels between blood donors and the general populations. This raises two questions: How comparable are HCV infection levels between blood donors and the general population in MENA? Are blood donor data, which are readily available, thanks to blood screening, an appropriate proxy for the general population in this region?

In this context, objectives of this study were to delineate HCV epidemiology in blood donors and general populations in MENA, and to assess how representative blood donor data are of HCV antibody (Ab) prevalence in the general population of this region. The study was also conducted to infer programmatic implications on blood safety in the region. These objectives were accomplished through analyses of a large, systematically gathered database, including 2622 HCV Ab prevalence measures on 49.8 million individuals by: (1) Estimating the pooled mean prevalence among blood donors and in general populations (henceforth the general population); and (2) Identifying predictors and trends of prevalence in these populations and sources of between-study heterogeneity. We further conducted

similar analyses for Europe, a region in which stringent donor selection and blood safety processes have been implemented[19], for comparison. We did so by utilizing a large systematically gathered database including 419 HCV Ab prevalence measures for 25.7 million individuals[20], to compare outcomes with results for MENA.

MATERIALS AND METHODS

Data sources

This study was conducted as part of the MENA HCV Epidemiology Synthesis Project[1], an ongoing project with the aim of delineating HCV epidemiology and informing key public health research, policy, and programming priorities in MENA. The source of data was the MENA HCV Epidemiology Synthesis Project Database[1]. The database included 685 HCV Ab prevalence measures on 46 634 214 blood donors and 528 measures on 2 358 944 individuals of the general population, such as pregnant women, healthy adults, and children. The database also included eight HCV viremic rate measures on 58 986 blood donors and 76 measures on 14 936 individuals of the general population. HCV viremic rate was defined as the proportion of those who had tested Ab positive that are subsequently confirmed to be chronically infected by testing positive for HCV RNA – the proportion of those HCV RNA positive among HCV Ab-positive individuals[21,22].

The database was populated through a series of systematic reviews for HCV infection across MENA that were previously conducted as part of this project[5,6,8,23-28]. All reviews followed a standardized methodology, and specific details such as literature search strategy, databases searched, and eligibility criteria can be found in each of these reviews[5,6,8,23-28]. The methodology used for these reviews was informed by the Cochrane Collaboration Handbook[29], and all findings were reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)[30]. Literature searches were conducted to identify primary data on HCV measures in international and national/regional databases, the MENA HIV/AIDS Epidemiology Synthesis Project Database[31,32], abstract archives of international conferences, and grey literature, including public health reports and routine data reporting. Literature searches were broad, with no language restrictions to ensure inclusiveness. All records reporting HCV measures after 1989, the year in which the virus was officially identified[33], were included in the reviews[5,6,8,23-28].

Blood donors are typically a diverse group with different rates of HCV Ab prevalence depending on the rigor of the donor selection process[19]. The vast majority of HCV Ab prevalence studies in MENA did not specify the type of blood donors, and therefore the term blood donors in the present analysis encompassed the different blood donor types, including regular voluntary nonremunerated donors, one-time voluntary nonremunerated donors, family replacement donors, and paid donors.

For the MENA HCV Epidemiology Synthesis Project, the MENA region was defined to include 24 countries (Figure 1). Given the distinctive nature of the HCV epidemics in Egypt[4-7] and Pakistan[8-11], relative to other MENA countries, separate analyses were performed for each of these countries.

HCV measures in blood donors and the general population were also analyzed for Europe, a region in which stringent donor selection and blood safety regulations have been implemented for decades [19], for comparison with MENA outcomes. Europe's HCV Ab prevalence measures were retrieved from the Hepatitis C Prevalence Database of the European Centre for Disease Prevention and Control [20]. The database was populated through a systematic review[16] and multiple reports[34,35]. The database included 257 HCV Ab prevalence measures on 25 232 790 blood donors and 120 measures on 410 444 individuals of the general population, such as pregnant women and healthy adults.

Pooled mean HCV Ab prevalence and viremic rate

Meta-analyses for countries and subregions were performed to pool HCV Ab prevalence in blood donors and the general population, whenever three or more measures were available, and a minimum sample size of 25 participants was met. Random-effects meta-analyses were performed using the DerSimonian–Laird method[36], with inverse-variance weighting to pool measures[36]. Freeman–Tukey type arcsine square-root transformation was used to stabilize the variance of each measure, factoring knowledge regarding the applicability of this transformation[37,38]. Heterogeneity was formally assessed[36]. Forest plots were generated and examined visually, and Cochran's Q-test was conducted. Statistical significance of heterogeneity was indicated whenever P was < 0.10[36,39]. The I^2 and its confidence interval (CI) were calculated to assess the percentage of variance that is explained by true differences in prevalence across studies, rather than chance[36]. Prediction intervals were also determined to describe the distribution of prevalence around the pooled mean estimate[36]. Meta-analyses were also used to estimate the pooled mean HCV viremic rate among blood donors and in the general population. Meta-analyses and forest plots were generated using R version 3.4.3.

Predictors, trends, and sources of between-study heterogeneity

Univariable and multivariable random-effects meta-regressions were conducted following established methodology[29]. A priori relevant independent variables in meta-regressions included subpopulation
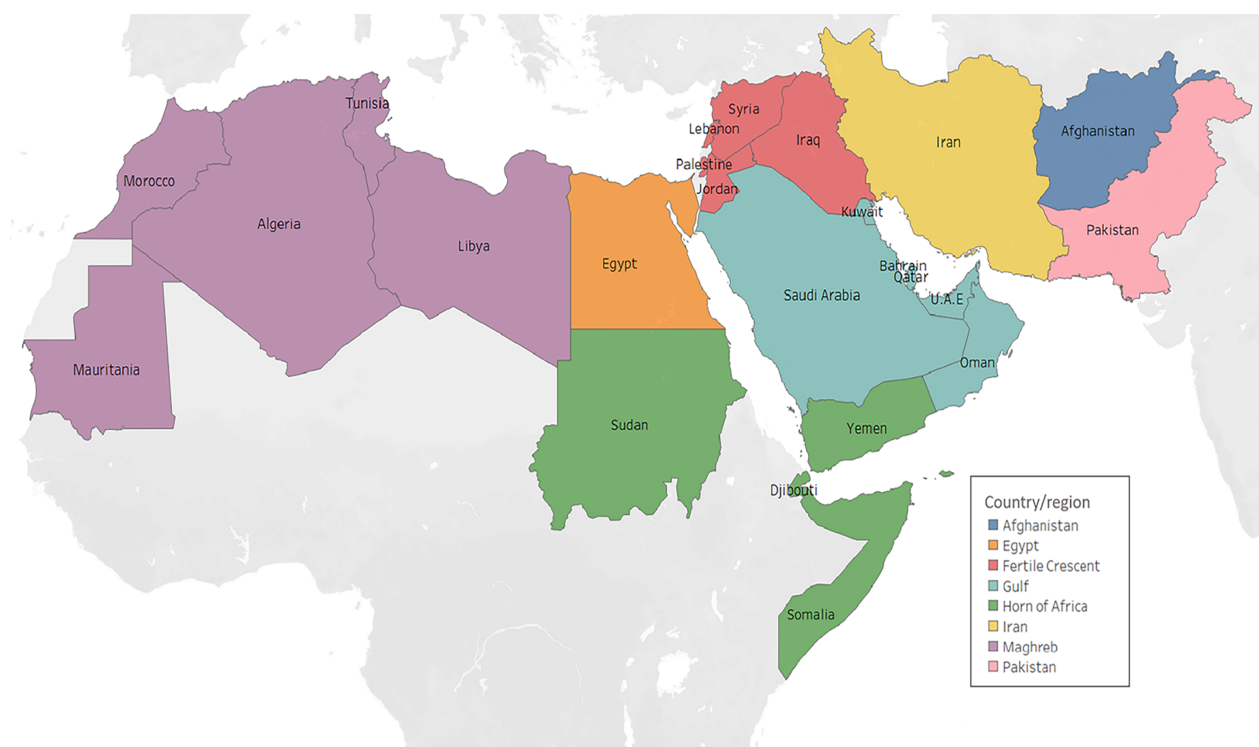
Figure 1 Map of the countries and subregions included in the Middle East and North Africa Region.

(blood donors *vs* the general population), country/subregion, and year of data collection. Factors associated with HCV Ab prevalence at $P \leq 0.20$ in the univariable analysis qualified for inclusion in the multivariable analysis. Here, an adjusted relative risk (ARR) $P \leq 0.05$ was considered to indicate strong evidence for an association.

In studies in which the year of data collection variable was missing, the variable was imputed. This was done by first subtracting the year of data collection (when available) from the year of publication for each study, and using the median of these values in imputing the year of data collection. Sensitivity analysis was performed without the imputed observations to determine the impact of the imputation on the results, confirming the results of the original meta-regression. Meta-regressions were performed on STATA version 13 using the *metan* command.

RESULTS

HCV Ab prevalence among blood donors and the general population in MENA

Studies on HCV Ab prevalence among blood donors and the general population in MENA are listed in Supplementary Tables 1 and 2. HCV Ab prevalence data were available for 23 of the 24 MENA countries. The largest number of data points were retrieved from Egypt, followed by the Gulf and Fertile Crescent Subregions. HCV Ab prevalence in blood donors ranged from 0 to 38.20%, with a median of 0.86% (Table 1). Studies reporting the highest HCV Ab prevalence were reported from parts of Egypt in the 1990s, a period during which HCV infection was widespread following the parenteral antischistosomal therapy (PAT) campaigns that contributed in a major way to the HCV epidemic in Egypt[5-7,40]. The pooled mean prevalence was 1.58% (95%CI: 1.48%–1.69%). It was lowest in the Fertile Crescent Subregion at 0.21% (95%CI: 0.18%–0.25%) and highest in Egypt at 10.40% (95%CI: 9.59%–11.23%), followed by Pakistan at 3.47% (95%CI: 2.96%–4.02%). HCV Ab prevalence in the general population ranged from 0 to 73.38%, with a median of 3.14%. The pooled mean prevalence was 4.49% (95%CI: 4.10%–4.90%). It was lowest in Iran at 0.33% (95%CI: 0.21%–0.47%) and highest in Egypt at 13.08% (95%CI: 11.51%–14.73%), followed by Pakistan at 8.81% (95%CI: 7.62%–10.06%). All outlier high HCV Ab prevalence measures were investigated and found to reflect blood donors or general populations in specific settings that were affected by high exposure to the virus, such as specific villages in the Nile delta in Egypt following the PAT era[5-7,40]. There was strong evidence for heterogeneity in HCV Ab prevalence in all meta-analyses ($P < 0.01$), with almost all variation being attributed to true variation in prevalence across studies rather than chance ($I^2 > 99.4\%$). Heterogeneity was also confirmed by the estimated prediction intervals (Table 1).

Table 1 Results of meta-analyses on studies reporting HCV Ab prevalence among blood donors and in the general population in Middle East and North Africa

Population	Studies	Samples	HCV Ab prevalence		Pooled HCV Ab prevalence		Heterogeneity measures		
	Total (*n*)	Total (*n*)	Range (%)	Median (%)	Mean (%)	95%CI	Q (*P* value)[1]	*I*[2] (confidence limits)[2]	Prediction interval (%)[3]
Blood donors									
Afghanistan	40	737407	0.00-7.19	0.60	0.75	0.57-0.96	3046.03 (*P* < 0.01)	98.7% (98.6%-98.9%)	0.02-2.41
Egypt	116	1566669	0.00-38.20	10.97	10.40	9.59-11.23	24513.7 (*P* < 0.01)	99.5% (99.5%-99.6%)	3.64-19.96
Fertile Crescent[4]	157	3488952	0.00-3.95	0.27	0.21	0.18-0.25	3674.2 (*P* < 0.01)	95.8% (95.4%-96.1%)	0.00-0.67
Gulf[5]	156	20891379	0.00-27.19	0.89	0.78	0.71-0.86	29882.0 (*P* < 0.01)	99.5% (99.5%-99.5%)	0.20-1.69
Horn of Africa[6]	22	48076	0.0-6.03	1.0	0.97	0.57-1.45	327.8 (*P* < 0.01)	93.6% (91.5%-95.2%)	0.00-3.78
Iran	73	15971802	0.00-3.13	0.24	0.31	0.22-0.40	55740.9 (*P* < 0.01)	99.9% (99.9%-99.9%)	0.00-1.43
Maghreb[7]	49	2145044	0.11-6.58	0.65	0.68	0.49-0.91	13475.9 (*P* < 0.01)	99.6% (99.6%-99.7%)	0.00-2.82
Pakistan	73	1797644	0.01-20.79	3.00	3.47	2.96-4.02	24753.7 (*P* < 0.01)	99.7% (99.7%-99.7%)	0.38-9.32
All countries/subregions	686	46646973	0.00-38.2	0.86	1.58	1.48-1.69	481819.0 (*P* < 0.01)	99.9% (99.9%-99.9%)	0.01-5.18
General population									
Afghanistan	6	12048	0.00-4.03	0.88	0.61	0.20-1.18	21.7 (*P* < 0.01)	76.9% (48.5%-89.6%)	0.00-2.68
Egypt	147	110603	0.00-54.10	11.82	13.08	11.51-14.73	8457.0 (*P* < 0.01)	98.3% (98.1-98.4%)	0.62-36.45
Fertile Crescent[4]	64	189456	0.00-8.87	0.19	0.42	0.24-0.64	1117.8 (*P* < 0.01)	94.4% (93.4%-95.2%)	0.00-2.39
Gulf[5]	85	222829	0.00-22.54	0.83	1.41	1.0-1.88	5343.3 (*P* < 0.01)	98.4% (98.3%-98.6%)	0.00-7.66
Horn of Africa[6]	27	29552	0.00-8.50	1.53	1.86	1.26-2.57	262.0 (*P* < 0.01)	90.1% (86.8%-92.6%)	0.00-6.13
Iran	50	101677	0.00-2.35	0.45	0.33	0.21-0.47	206.9 (*P* < 0.01)	76.3% (69.0%-81.9%)	0.00-1.25
Maghreb[7]	42	1378206	0.00-6.16	0.62	0.87	0.55-1.26	7595.3 (*P* < 0.01)	99.5% (99.5%-99.5%)	0.00-4.38
Pakistan	106	301814	0.44-73.38	6.82	8.81	7.62-10.06	13619.0 (*P* < 0.01)	99.2% (99.2%-99.3%)	0.60-24.62
All countries/subregions	527	2346185	0.00-73.38	3.14	4.49	4.10-4.90	83750.3 (*P* < 0.01)	99.4% (99.4%-99.4%)	0.00-16.88

[1]Q: the Cochran's Q statistic is a measure assessing the existence of heterogeneity in effect size (here, HCV Ab prevalence) across studies.

[2]*I*[2]: A measure assessing the magnitude of between-study variation that is due to true differences in effect size (here, HCV Ab prevalence) across studies rather than chance.

[3]Prediction interval: a measure estimating the 95% interval of the distribution of true effect sizes (here, HCV Ab prevalence).

[4]Countries include Iraq, Jordan, Lebanon, Palestine, and Syria.

[5]Countries include Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and United Arab Emirates.

[6]Countries include Djibouti, Somalia, Sudan, and Yemen.

[7]Countries include Algeria, Libya, Mauritania, Morocco, and Tunisia. Ab: Antibody; CI: Confidence interval; HCV: Hepatitis C virus.

HCV Ab prevalence among blood donors and the general population in Europe

HCV Ab prevalence data were available for 30 countries in Europe. HCV Ab prevalence in blood donors ranged from 0 to 3.28%, with a median of 0.06% (Table 2). The pooled mean prevalence was 0.11%

Table 2 Results of meta-analyses on studies reporting HCV Ab prevalence among blood donors and in the general population in Europe

Subpopulation	Studies	Samples	HCV Ab prevalence		Pooled HCV Ab prevalence		Heterogeneity measures		
	Total (*n*)	Total (*n*)	Range (%)	Median (%)	Mean (%)	95%CI	Q (*P* value)[1]	*I*[2] (confidence limits)[2]	Prediction interval (%)[3]
Blood donors	257	25232790	0.0-3.28	0.06	0.11	0.10-0.13	35657.5 (*P* < 0.01)	99.3 (99.3-99.3)	0.00-0.51
The general population	120	410444	0.0-16.83	1.11	1.59	1.25-1.97	9176.9 (*P* < 0.01)	98.7 (98.6-98.8)	0.0-7.57

[1]Q: the Cochran's Q statistic is a measure assessing the existence of heterogeneity in effect size (here, HCV Ab prevalence) across studies.

[2]I^2: a measure assessing the magnitude of between-study variation that is due to true differences in effect size (here, HCV Ab prevalence) across studies rather than chance.

[3]Prediction interval: a measure estimating the 95% interval of the distribution of true effect sizes (here, HCV Ab prevalence). Ab: Antibody; CI: Confidence interval; HCV: Hepatitis C virus.

(95%CI: 0.10%–0.13%). Prevalence in the general population ranged from 0 to 16.83%, with a median of 1.11%. The pooled mean prevalence was 1.59% (95%CI: 1.25%–1.97%). There was strong evidence for heterogeneity in HCV Ab prevalence ($P < 0.01$), with the majority of variation being attributed to true variation in prevalence across studies rather than chance ($I^2 > 98.7\%$).

HCV viremic rate of blood donors and the general population

The HCV viremic rate of blood donors in different MENA countries ranged from 61.84% to 93.33%, with a median of 70.78% (Supplementary Table 3). The pooled mean for the entire MENA region was 76.29% (95%CI: 67.64%–84.02%), indicating that approximately three-quarters of Ab-positive blood donors are chronically infected. The viremic rate ranged from 22.73% to 100% in the general population in different MENA countries, with a median of 68.27% (Supplementary Table 3). The pooled mean for the entire MENA region was 65.73% (95%CI: 61.03%–70.29%). There was strong evidence for heterogeneity in the viremic rates ($P < 0.01$), with most variation being attributed to true variation in the viremic rate across studies rather than chance ($I^2 > 77.4\%$).

Predictors and trends of HCV Ab prevalence in MENA

The meta-regressions for MENA indicated that HCV Ab prevalence in the general population was 1.72-fold (95%CI: 1.50–1.97) higher than that in blood donors (Table 3). They also indicated substantial variation in prevalence by country and subregion with Egypt and Pakistan having a higher prevalence than the rest of MENA countries. Importantly, the analyses indicated that HCV Ab prevalence has been declining over the last three decades at an average rate of 4% per year (ARR of 0.96; 95%CI: 0.95–0.97). Subgroup analyses were conducted on the above results. The same regressions were repeated, but for Egypt, Pakistan and other MENA countries individually (Table 4). These analyses indicated that HCV Ab prevalence in the general population was 1.30-fold (95%CI: 1.07–1.59) higher than that among blood donors in Egypt, 2.52-fold (95%CI: 1.89–3.36) higher in Pakistan, and 1.73-fold (95%CI: 1.42–2.11) higher in the remaining MENA countries. The analyses also confirmed the same rate of decline for prevalence at 4% in the rest of MENA countries. The rate of decline was slightly higher in Egypt at 6%. There was no evidence for a decline in prevalence, however, in Pakistan.

In a sensitivity analysis, the same regressions were also repeated, but excluding all blood donor data (not shown). The analyses indicated that HCV Ab prevalence in MENA is declining at a rate of 5% per year (ARR of 0.95; 95%CI: 0.93–0.97), indicating a marginally higher rate of decline in the general population.

Predictors and trends of HCV Ab prevalence in Europe

The meta-regressions for Europe indicated that HCV Ab prevalence in the general population is 15.10-fold (95%CI: 11.48–19.86) higher than that in blood donors (Table 5). The analyses indicated further that HCV Ab prevalence has been declining over the last three decades at a similar rate to that of MENA, at 4% per year (ARR of 0.96; 95%CI: 0.92–0.99).

A sensitivity analysis was conducted on the above results. The same regressions were repeated, but excluding all blood donor data (not shown). The analyses indicated that HCV Ab prevalence in Europe is declining at a rate of 10% per year (ARR of 0.90; 95%CI: 0.85–0.96), higher than that in MENA.

Table 3 Univariable and multivariable meta-regression models for HCV Ab prevalence among blood donors and the general population in Middle East and North Africa

	Studies	Samples	Univariable analysis				Multivariable analysis[b]	
	Total (*n*)	Total (*n*)	RR (95%CI)	*P* value	F *P* value[a]	Variance explained R^2 (%)	ARR (95%CI)	*P* value
Subpopulations								
Blood donors	686	46646973	1	-			1	-
The general population	527	2346185	2.92 (2.41-3.55)	< 0.001	< 0.001	10.73	1.72 (1.50-1.97)	< 0.001
Country/subregion								
Afghanistan	46	749455	1	-			1	-
Egypt	263	1677272	14.89 (10.2-21.8)	< 0.001			9.48 (6.54-13.75)	< 0.001
Fertile Crescent[1]	221	3678408	0.52 (0.35-0.77)	< 0.001			0.49 (0.34-0.72)	< 0.001
Gulf[2]	241	21114208	1.24 (0.84-1.82)	0.280			0.82 (0.56-1.19)	0.398
Horn of Africa[3]	49	77628	2.05 (1.25-3.37)	0.005			1.33 (0.82-2.15)	0.244
Iran	123	16073479	0.50 (0.33-0.77)	< 0.001			0.42 (0.28-0.63)	< 0.001
Maghreb[4]	91	3523250	1.02 (0.66-1.56)	0.936			0.77 (0.51-1.16)	0.207
Pakistan	179	2099458	6.96 (4.71-10.29)	< 0.001	< 0.001	58.39	5.44 (3.73-7.93)	< 0.001
Year of data collection	1213	48993158	0.95 (0.94-0.97)	< 0.001	< 0.001	3.71	0.96 (0.95-0.97)	< 0.001

[1]Countries include Iraq, Jordan, Lebanon, Palestine, and Syria.

[2]Countries include Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and United Arab Emirates.

[3]Countries include Djibouti, Somalia, Sudan, and Yemen.

[4]Countries include Algeria, Libya, Mauritania, Morocco, and Tunisia.

[a]Variables with *P* ≤ 0.2 were eligible for inclusion in the multivariable analysis.

[b]The adjusted R-squared for the full model was 62.65%.

Ab: Antibody; ARR: Adjusted relative risk; CI: Confidence interval; RR: Relative risk.

DISCUSSION

Levels and trends of HCV Ab prevalence in blood donors and in the general population of MENA were assessed using a large standardized database. There was large variability in HCV Ab prevalence by country and subregion, with Egypt and Pakistan, the largest countries in MENA by population size, having several fold higher prevalence than the rest of MENA countries. HCV Ab prevalence in the remaining MENA countries was at about 1% or less, similar to that in Europe and most other countries globally[12,41]. These results confirm our understanding of HCV epidemiology across MENA countries and subregions[4-11,21-28,42-49].

Strikingly, HCV Ab prevalence is declining rapidly in both MENA and Europe, and at a similar rate of about 4% per year. The exception to this downward trend was Pakistan where there was no evidence for a decline. These declines may be reflective, in part, of the declining incidence of HCV infection within these regions through improvements to infection control following the discovery of this virus three decades ago, and scale-up of HCV treatment worldwide[3]. They also may reflect the progressive improvement in effective blood donor selection, such as by motivating and retaining voluntary nonremunerated donors to donate regularly[19].

A major finding of this study is that HCV Ab prevalence in blood donors in MENA was similar to HCV Ab prevalence in the general population; unlike the situation in Europe. While HCV Ab prevalence in the general population was almost twofold higher than that of HCV Ab prevalence in blood donors in MENA, it was 15-fold higher in Europe (Table 3 *vs* Table 5). HCV Ab prevalence in blood donors in MENA appears to closely reflect the background prevalence in the wider population. Of note that HCV Ab prevalence in blood donors is a function of not only the prevalence in the general

Table 4 Subgroup analyses: Univariable and multivariable meta-regression models for HCV Ab prevalence among blood donors and the general population in Egypt, Pakistan, and rest of Middle East and North Africa countries

	Studies	Samples	Univariable analysis				Multivariable analysis[b]	
	Total (*n*)	Total (*n*)	RR (95%CI)	*P* value	F *P* value[a]	Variance explained R² (%)	ARR (95%CI)	*P* value
Egypt								
Subpopulations								
Blood donors	116	1566669	1	-			1	-
The general population	147	110603	1.25 (1.00-1.57)	0.049	0.087	2.05	1.30 (1.07-1.59)	0.008
Year of data collection	263	1677272	0.94 (0.93-0.95)	< 0.001	< 0.001	24.48	0.94 (0.93-0.95)	< 0.001
Pakistan								
Subpopulations								
Blood donors	73	1797644	1	-			-	-
The general population	106	301814	2.52 (1.89-3.36)	< 0.001	< 0.001	19.03	-	-
Year of data collection	179	2099458	1.00 (0.98-1.03)	0.648	0.648	0.00	-	-
Rest of MENA countries								
Subpopulations								
Blood donors	497	43282660	1	-	-		1	-
The general population	274	1933768	1.80 (1.47-2.21)	< 0.001	< 0.001	5.44	1.73 (1.42-2.11)	< 0.001
Country/subregion								
Afghanistan	46	749455	1	-	-		1	-
Fertile Crescent[1]	221	3678408	0.53 (0.35-0.81)	0.003			0.50 (0.33-0.75)	0.001
Gulf[2]	241	21114208	1.26 (0.83-1.91)	0.273			0.86 (0.56-1.30)	0.462
Horn of Africa[3]	49	77628	2.08 (1.22-3.54)	0.007			1.37 (0.81-2.32)	0.247
Iran	123	16073479	0.51 (0.33-0.81)	0.004			0.43 (0.28-0.67)	< 0.001
Maghreb[4]	91	3523250	1.04 (0.65-1.64)	0.883	< 0.001	11.48	0.79 (0.50-1.24)	0.298
Year of data collection	771	45216428	0.95 (0.94-0.96)	< 0.001	< 0.001	6.22	0.96 (0.95-0.98)	< 0.001

[1]Countries include Iraq, Jordan, Lebanon, Palestine, and Syria.

[2]Countries include Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and United Arab Emirates.

[3]Countries include Djibouti, Somalia, Sudan, and Yemen.

[4]Countries include Algeria, Libya, Mauritania, Morocco, and Tunisia.

[a]Variables with a *P* value ≤ 0.2 were eligible for inclusion in the multivariable analysis. No multivariable analysis was conducted for Pakistan, as only one variable qualified for inclusion in the model.

[b]The adjusted R-squared was 27.35% for the multivariable model for Egypt and 17.92% for the multivariable model for rest of MENA countries. Ab: Antibody; ARR: Adjusted relative risk; CI: Confidence interval; RR: Relative risk.

population, but also of the effectiveness of blood donation programs to collect blood from regular voluntary nonremunerated blood donors[19]. This finding suggests that risk reduction strategies through selection and retention of safer blood donors (regular voluntary nonremunerated blood donors) are not yet effectively implemented widely in MENA as in Europe[19], where the source of blood largely comes from such donors. Indeed regulatory framework (including legislation, regulation, policies and standards) and a functioning regulatory authority to enforce the regulatory framework is largely at its infancy in MENA[19], where, as of 2016, only 55% of MENA countries had legislation covering safety and quality of blood transfusions, and only two countries had achieved 100% voluntary nonremunerated blood donations[19,50]. Furthermore, HCV Ab prevalence in blood donors may be reflective of people in the general population unaware of their HCV infection status, in the context of which an individual aware of their positive HCV infection status would not donate blood.

Nevertheless, contingent on the quality of blood donor management systems implemented within countries of MENA, this finding indicates that HCV Ab prevalence in blood donors in MENA (unlike in North America[18] and Europe[16]) can be used for the time being as a proxy to estimate infection levels in the general population. This outcome has important consequences. With the lack of nationally repres-

Table 5 Univariable and multivariable meta-regression models for HCV Ab prevalence among blood donors and the general population in Europe

	Studies	Samples	Univariable analysis				Multivariable analysis[b]	
	Total (*n*)	Total (*n*)	RR (95%CI)	*P* value	F *P* value[a]	Variance explained R² (%)	ARR (95%CI)	*P* value
Subpopulations								
Blood donors	257	25232790	1				1	
The general population	120	410444	15.57 (11.83-20.49)	< 0.001	< 0.001	53.62	15.10 (11.48-19.86)	< 0.001
Year of data collection	377	25643234	0.93 (0.88-0.98)	0.004	0.005	2.17	0.96 (0.92-0.99)	0.020

[a]Variables with $P \leq 0.2$ were eligible for inclusion in the multivariable analysis.

[b]The adjusted R^2 for the full model was 54.27%.

Ab: Antibody; ARR: Adjusted relative risk; CI: Confidence interval; RR: Relative risk.

entative population-based surveys in most countries of this region, blood donor data, which are readily available, can be easily used to assess levels and trends of this infection in the wider population. They can also be used to generate other estimates, such as those related to the disease burden of HCV sequelae, and can be leveraged to assess, track and validate progress toward the WHO elimination goals for this infection[3]. The present study also provides adjustment factors to improve use of blood donor data (Table 2), so that they better reflect HCV levels in the wider population. These adjustment factors can be used at a regional level, or can be fine-tuned so as to be specific for individual countries.

This study had several limitations. Availability of data varied across MENA, with HCV Ab prevalence data being unavailable for Bahrain. The majority of HCV viremia data were collected at times before the launch of DAA treatment programs (Supplementary Table 3); thus, they may not represent the current viremic rate in blood donors and in the general population. Analysis for the different blood donor types was not conducted as the specification of blood donor type was not available for the vast majority of HCV Ab prevalence measures. The sample size of blood donors was larger than that of the general population; however, the sample size in the general population was still substantial at 2.3 million. Despite these limitations, an immense volume of data was acquired, allowing various analyses and an array of consequential inferences to be drawn. While high heterogeneity was found, most (63%) of it was subsequently explained in meta-regression analyses in terms of prevalence variation by country and subregion within MENA.

CONCLUSION

HCV Ab prevalence in the wider population of MENA and Europe appears to be rapidly declining by 4% per year. Blood donor data in MENA (but not in Europe) provide a useful proxy for HCV infection levels and trends in the general population; at least in countries where effective blood donor selection and blood donor management programs are not in place. Thus, the data can be utilized in HCV infection and disease burden estimates and to assess, track and validate progress toward WHO elimination goals for this infection. While these findings are specific for MENA, they may also apply to resource-limited countries of other regions.

ARTICLE HIGHLIGHTS

Research background

The Middle East and North Africa (MENA) Region is the most affected by hepatitis C virus (HCV) infection, with approximately 20% of the global chronically infected individuals residing in this region. Despite this, only three countries conducted national population-based surveys to delineate HCV infection levels in the general population.

Research motivation

HCV infection in blood donors have been used as a proxy for HCV infection levels in the general population. However, it is unclear how comparable blood donors are to the general population in countries in MENA and whether they are a suitable proxy population.

Research objectives

To delineate HCV epidemiology in blood donors and in the general population in MENA.

Research methods

The MENA HCV Epidemiology Synthesis Project Database was used as a data source. Studies reporting HCV in blood donors and in the general population were retrieved, and random-effects meta-analyses and random-effects meta-regressions were performed. For regional comparison, similar analyses were performed for countries in Europe, using the Hepatitis C Prevalence Database from the European Centre for Disease Prevention and Control (ECDC).

Research results

A total of 1213 HCV Ab prevalence measures and 84 viremic rate measures were retrieved from the MENA HCV Epidemiology Synthesis Project, and 377 HCV Ab prevalence measures were retrieved from the ECDC. The pooled mean prevalence in MENA was 1.58% [95% confidence interval (CI): 1.48%–1.69%] in blood donors and 4.49% (95%CI: 4.10%–4.90%) in the general population, and in Europe was 0.11% (95%CI: 0.10%–0.13%) among blood donors and 1.59% (95%CI: 1.25%–1.97%) in the general population. In MENA, the prevalence in the general population was 1.72-fold (95%CI: 1.50–1.97) higher than that in blood donors, and in Europe it was 15.10-fold (95%CI: 11.48–19.86) higher. HCV prevalence appeared to be declining by 4% annually in both MENA and Europe.

Research conclusions

Blood donor data in MENA (but not in Europe) appears to be comparable with that in the general population and therefore can be used as a useful proxy for HCV infection levels and trends in the general population, at least in countries where effective blood donor selection and blood donor management programs are not yet firmly in place. Blood donor data may be used to estimate HCV infection and disease burden and to assess, track, and validate progress toward World Health Organization elimination goals for this infection.

Research perspectives

With the lack of nationally representative population-based surveys in most countries in MENA and beyond, blood donor data, which are readily available, can be easily used to assess levels and trends of this infection in the wider population. The study rationalizes and facilitates generation of estimates at low costs and demands for resources, even in resource-limited settings where population-level data are most scarce. While these findings are specific for MENA, they may also apply and be of relevance to other global regions.

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FOOTNOTES

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